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Mechanical Ventilation In Neonates

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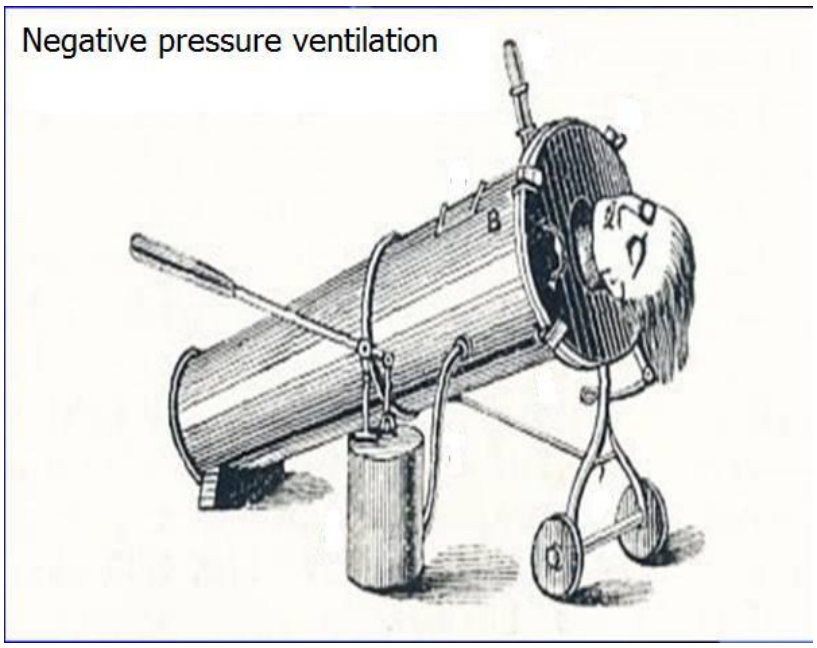
Introduction

The introduction of mechanical ventilation in neonatal medicine begin in 1960s.

It is a lifesaving therapy.

- 1904 Negative pressure ventilation.
- 1905 CPAP.
- 1907 positive pressure mechanical ventilation.
- 1960-1970 Birth neonatology.
- 1963 First baby successfully ventilated.



Positive pressure:

The aerophore plumonaire:

developed by French obstetrician for short term ventilation of newborn in 1879.

Goals of mchanical ventilation

1. Provide adequate oxygenation and ventilation with the most minimal intervention possible.
2. Minimize the risk of lung injury.
3. Reduce patient work of breathing (WOB).
4. Optimize patient comfort.

Indications of mechanical ventilation

At Birth:

- Failure to establish spontaneous respiration in spite of mask.
- Persistent bradycardia .
- Diaphragmatic hernia.
- Infant < 28 wks. G.A or < 1kg.
- Infant < 32 wks. G.A may be intubated to receive surfactant.

In the NICU:

- Respiratory failure and deterioration of blood gases
- (Po**2**≤60 in Fio2 70 or Pco**2**≥ 60).

Infant at risk of sudden collapse:

- Frequent apnea.
- Severe sepsis.
- Severe asphyxia.
- PPHN.
- Maintenance of patient airway (as choanal atresia , Pierr-robin syndrome).

Intubation

Elective Intubation

Use pre-medication

Equipment

- Suction
- Oxygen with pressure limiting device and T-piece or 500 mL bag and appropriate size mask
- ETT tubes 3 sizes (diameter in mm):

Weight of baby (g)	ETT
<1000–1250	2.5
1250–3000	3.0
>3000	3.5

- Hat for baby to secure tube, ETT fixing device, forceps and scissors.
- Laryngoscopes x 2, stethoscope, oropharyngeal airway.

Preparation

- Ensure cannula in place and working.
- Ensure all drugs drawn up, checked, labelled and ready to give.
- Check no contraindications to drugs.
- Ensure monitoring equipment attached and working reliably.
- If nasogastric tube (NGT) in place, aspirate stomach (particularly important if baby has been given enteral feeds).

Premedication

- Give 100% oxygen for 2 min before drug administration.
- Continue to give 100% oxygen until laryngoscopy and between attempts if more than one attempt necessary.

Drugs : (Page 8)

Choice of drugs depends on local practice
Analgesia and muscle relaxation can improve likelihood of successful intubation..

Muscle relaxants

Administer muscle relaxants only if you are confident that the team can intubate baby quickly. Do not use a muscle relaxant unless adequate analgesia has been given

Procedures

- Lift laryngoscope: do not tilt.
- Avoid trauma to gums.
- Cricoid pressure: by person intubating or an assistant.
- Suction secretions only if they are blocking the view as this can stimulate the vagal nerve and cause a bradycardia and vocal cord spasm.
- Insert ET tube (ETT).
- Advance ETT to desired length at the lips.
- General recommendation is to advance ETT no further than end of black mark at end of tube (2.5 cm beyond cords), but this length is far too long for extremely preterm babies.

See table: Length of ETT for where approximate markings of the ETT should be at the lips.

Table: Length of ETT

Gestation of baby	Actual weight of baby/kg	Length of ETT (cm) at lips
23-24	**0.5-0.6**	**5.5**
25-26	**0.7-0.8**	**6.0**
27-29	**0.9-1.0**	**6.5**
30-32	**1.1-1.4**	**7.0**
33-34	**1.5-1.8**	**7.5**
35-37	**1.9-2.4**	**8.0**
38-40	**2.5-3.1**	**8.5**
41-43	**3.2-4.2**	**9.0**

- Remove stylet if used and check to ensure it is intact before proceeding.
- If stylet not intact, remove ETT immediately and prepare to reintubate.
- Auscultate chest to check for bilateral equal air entry.
- If air entry unequal and louder on right side, withdraw ET by 0.5 cm and listen again.
- Repeat until air entry equal bilaterally.

Do not leave baby with unequal air entry

- stabilise tube using ETT fixation method in accordance with unit practice.
- request chest X-ray: adjust ETT length so that tip is at level of T1–2 vertebrae and document on nursing chart and in baby's hospital notes.

Intubation failure

Definition: Unable to intubate within 30 seconds

- If intubation unsuccessful, seek help from someone more experienced.
- If there is a risk of aspiration, maintain cricoid pressure.
- Continue bag and mask ventilation with 100% oxygen until successful intubation achieved.

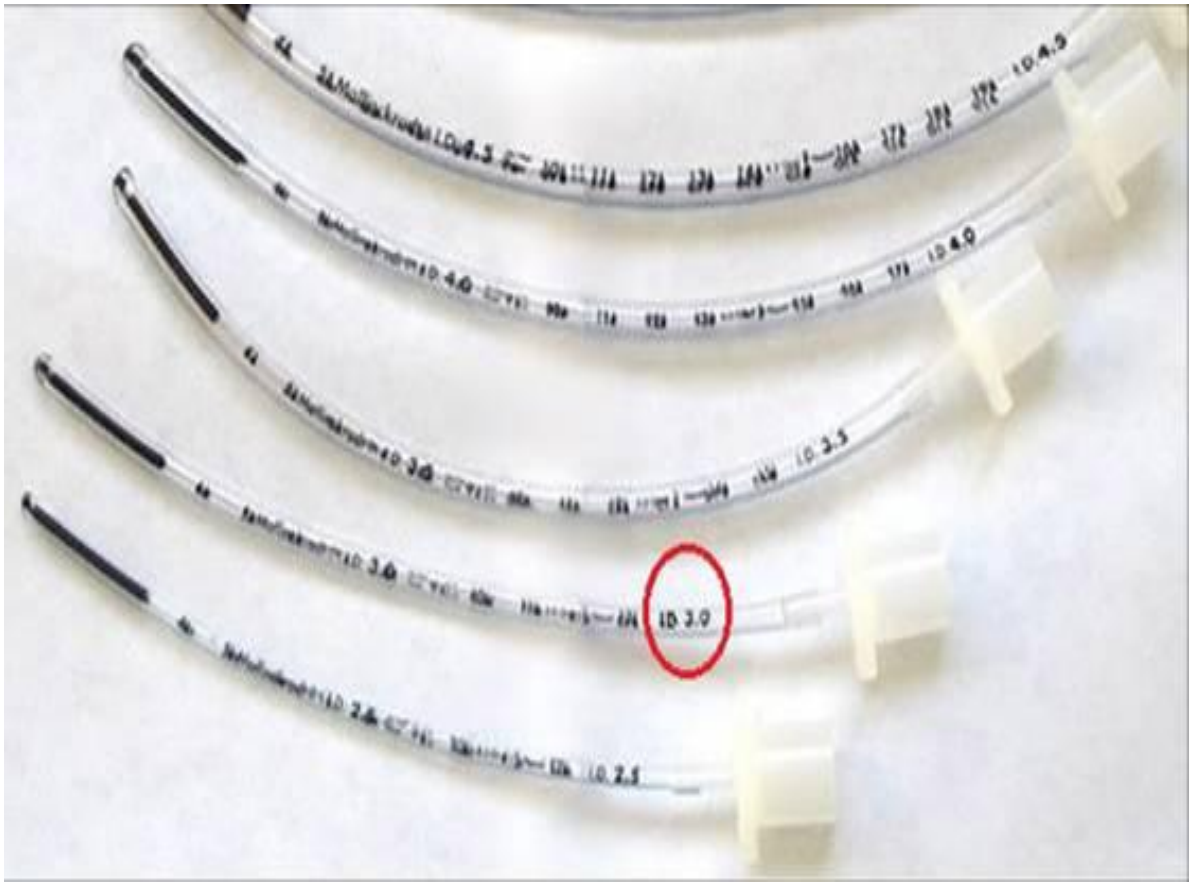
Depth of E.T.T

- Insertion = weigh + 6 .

Size of E.T.T

- 1/10 G.A in wks .

Example : G.A 35 wks , so size of E.T.T 35/10=3.5



Different size of E.T.T. I.D (Internal Diameter in mm)

Sedation & muscle relaxation

Fentanyl :

- IV 1-4 microgram /kg/dose 2-4 hrs.
- Infusion 1-5 microgram/kg/hr

  50 microgram /kg +50ml D5%

  Give 1 microgram/ kg/hr = 1ml /kg /hr.

Midazolam :

- IV 100-200 microgram/kg/dose 4-8hrs.
- Infusion 20-60 microgram/kg/hr.

How many Midazolam in mg added to 50ml D5% =

$$= \frac{50 \times wt \times \text{dose in microgram}}{\text{I.V Rate (ml/hr)}}$$

Muscle relaxant :

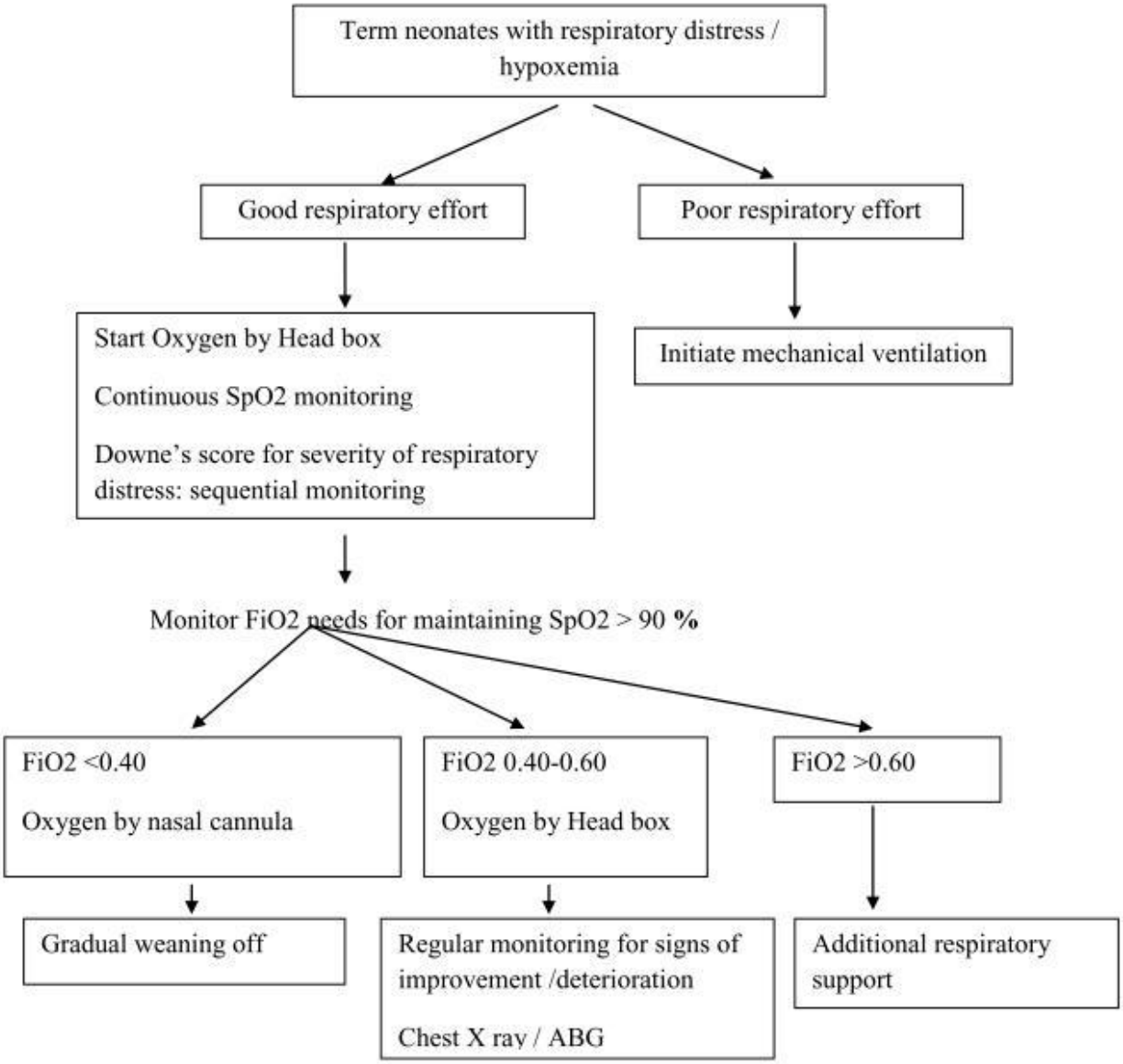
Used when the infant breaths out of phase with the ventilation in spite of sedation .

- Pancuronium (0.1mg/kg/dose)repeated as needed .

N.B Also limiting environmental light and noise help to make infant more relax.

Algorithm for oxygen therapy in newborns

The algorithm for term babies needing oxygen therapy has been mentioned bellow. The preterm babies with respiratory distress from a separate group, as they may need early CPAP and surfactant therapy.



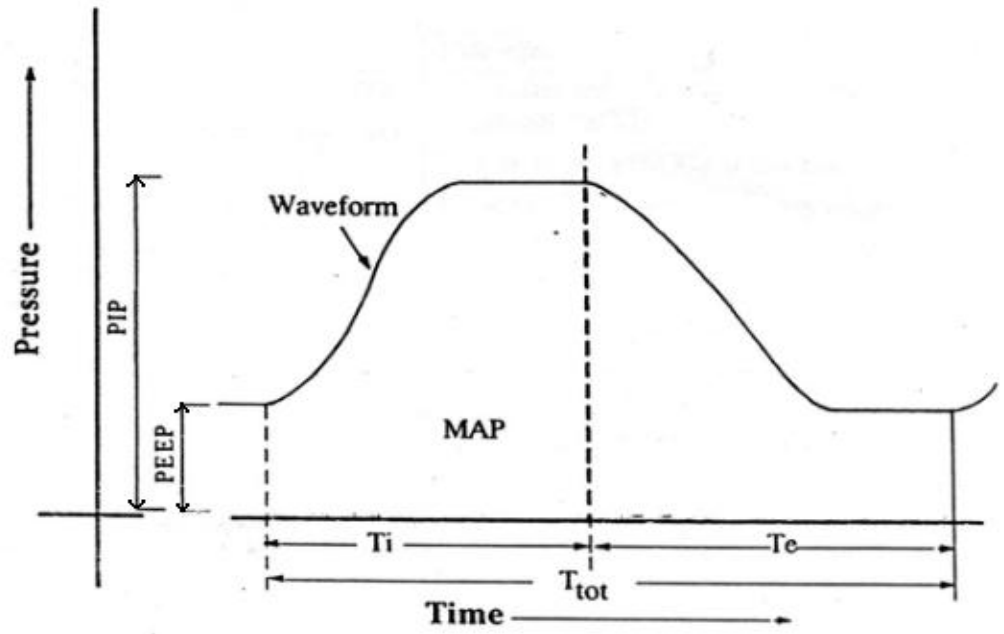
Basic Terminology Mechanical Ventilation

CO2 Elimination :

- Alveolar ventilation = (Tidal volume – Dead space) x Respiratory rate/min
- Volume-controlled ventilator : Preset Tidal volume
- Pressure-limited : lung compliance, Pressure gradient (PIP - PEEP)

O2 Uptake :

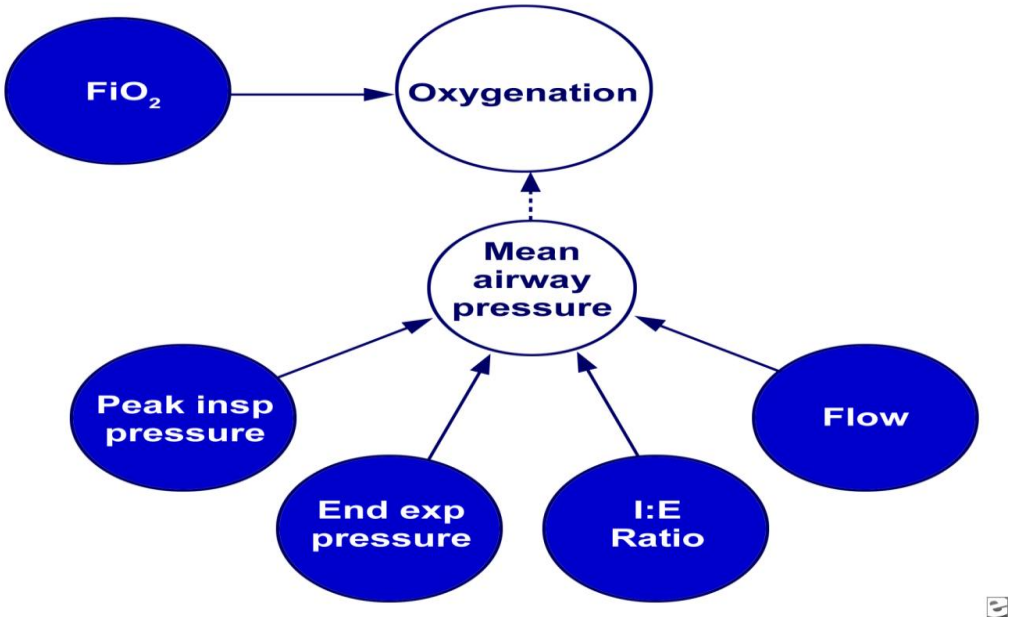
- Depends on Mean Airway pressure (MAP)
- MAP - Area under airway pressure curve divided by duration of the cycle
- MAP = K (PIP – PEEP) [Ti/(Ti + Te)] + PEEP



MAP :

MAP can be augmented by:

- Inspiratory flow rate (increases K)
- Increasing PIP
- Increasing I:E ratio
- Increasing PEEP



Conventional Ventilator Settings

The key settings are:

- FIO2
- PIP
- PEEP
- RR
- I:E ratio
- Flow rate

MAP – net outcome of all parameters except Fio2 and RR; true measure of average pressure; should be maintained between 8-12 cm H20 .

FIO2:

$$FIO2 = \frac{O2\ Flow + (0.21 \times air\ Flow)}{Total\ Flow}$$

Example: O2 Flow = 6

Air Flow = 4

$$\frac{6 + 0.84}{10} = 0.68$$

- Inspired oxygen concentration
- Fraction of O2 in inspired air-oxygen mixture
- Regulated by blenders
- Fio2 – kept at a minimum level to maintain PaO2 of 50-80 mm Hg.
- Initial Fio2 – 0.5 – 0.7

Peak Inspiratory Pressure (PIP)

Neonate with normal lung requires PIP of about 12 cm H2O for ventilation.

- Appropriate to start with PIP of 18-20 cm H2O for mechanical ventilation.
- Primary variable determining tidal volume.
- High PIP – Barotrauma.

Positive End Expiratory Pressure (PEEP)

Most effective parameter that increases MAP.

- Has opposite effects on CO2 elimination.
- PEEP range of 4-8 cm H2O is safe and effective.
- Excess PEEP decreases compliance, increase pulmonary vascular resistance.

Respiratory Rate (RR)

- Main determinant of minute ventilation.
- Rate to be kept within normal range or higher than normal rate, especially at the start of mechanical ventilation.
- Hyperventilation – used in treatment of PPHN.

I:E Ratio (Inspiratory-Expiratory ratio)

Primarily effects MAP and oxygenation

- Physiological ratio : 1:1 or 1:1.5
- Reversed ratio (2:1 or 3:1) – FiO2 and PEEP can be reduced.
- Prolonged expiratory rates (1:2 or 1:3) – MAS and during weaning.

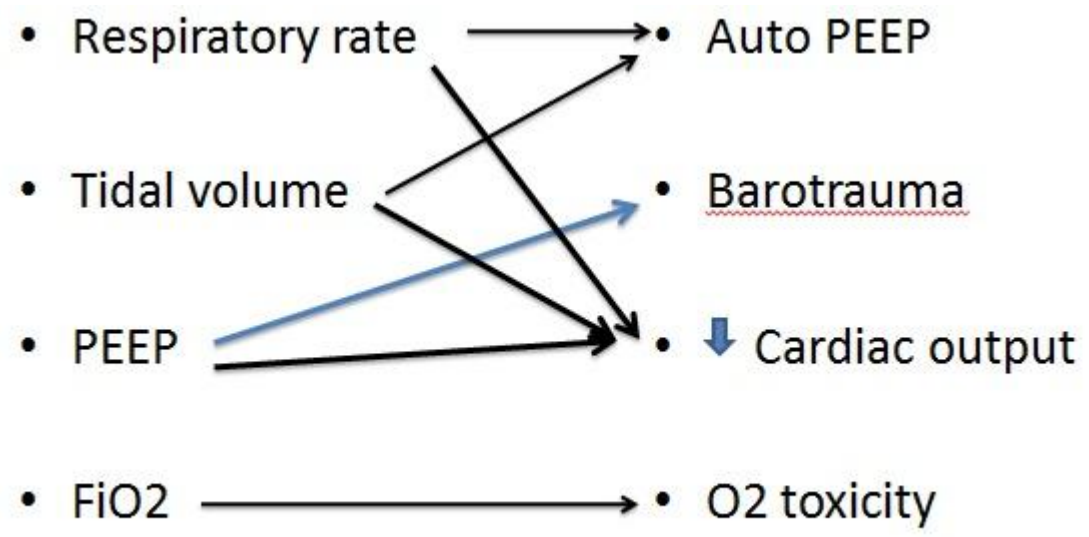
$$\text{Total breath Time} = \frac{60 \text{ sec}}{\text{Breath Rate}}$$

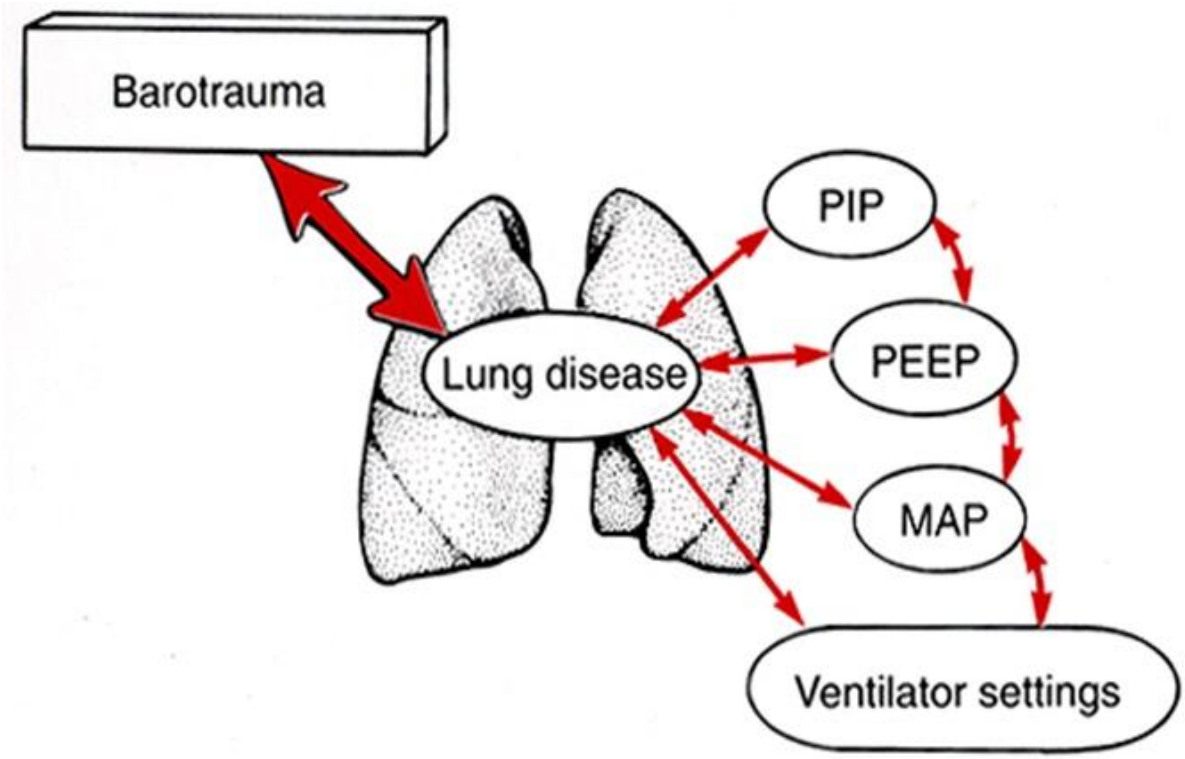
Example Rate = 30 , Total time 60/30 = 2 sec.

If Ti = 0.4 so TE = 1.6 sec .

Flow Rate

- Usually flow rate of 4-8 L/min is sufficient
- Minimum flow of at least two times minute ventilation volume is required
- High-flow rate – increased risk of alveolar rupture





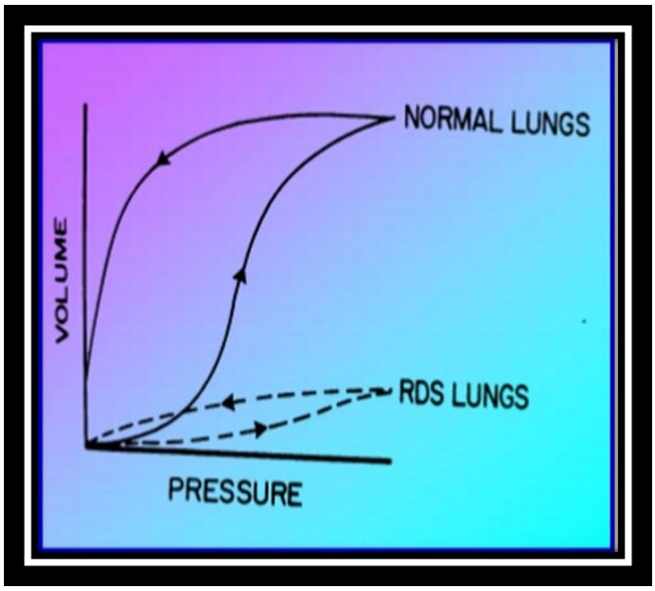
Lung physiology and mechanics

Neonatal Respiratory Physiology

Compliance:

- Distensible nature of lungs and chest wall.

$$\text{Volume (L)} = \frac{\text{Volume (L)}}{\text{Pressure (cm } H_2O\text{)}}$$



- Neonates have greater chest wall compliance. (premature more than FT)
- Premature infants with RDS have stiffer lungs (poorly compliant lungs).

Normal infant 0.003 to 0.006 L/cmH2O.

In RDS 0.0005 to 0.001 L/cmH2O.

Resistance:-

- Property of airways and lungs to resist gas.

$$\text{Resistance} = \frac{\Delta \text{ Pressure (cm } H_2O)}{\Delta \text{ Flow (L/sec)}}$$

- Resistance in infants with normal lungs ranges from 25 to 50 cm H2O/L/sec.
- It is increased in intubated babies and ranges from 50 to 100 cm H2O/L/sec.

Total respiratory system resistance =

chest wall R (25%)+ airway R (55%)+ lung tissue R (20%).

Neonatal Respiratory Physiology

Time Constant:

An index of how rapidly the lungs can empty.

Time constant = Compliance X Resistance

- In BPD time constant is long because of ↑ resistance.
- In RDS time constant is short because of low compliance.
- Normal = 0.12-0.15 sec.

Time Constant

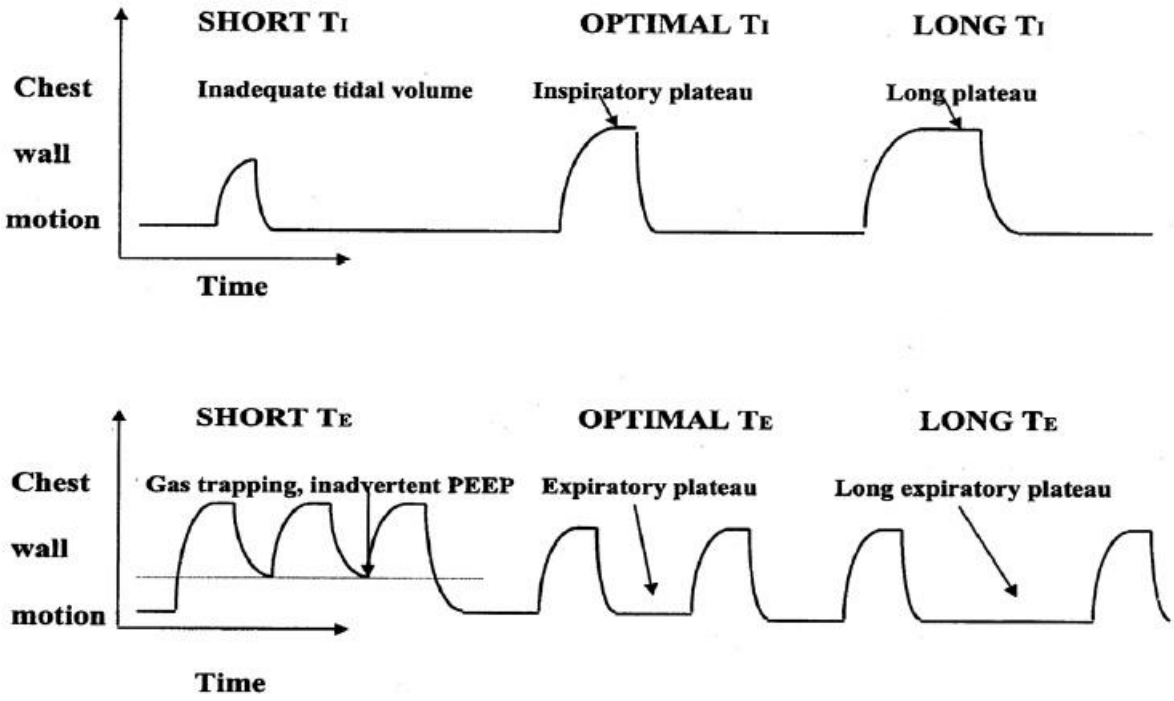
Inspiratory time must be 3-5 X time constant

- One time constant = time for alveoli to discharge 63% of its volume through the airway.
- Two time constant = 84% of the volume leaves.
- Three time constant = 95% of volume leaves.

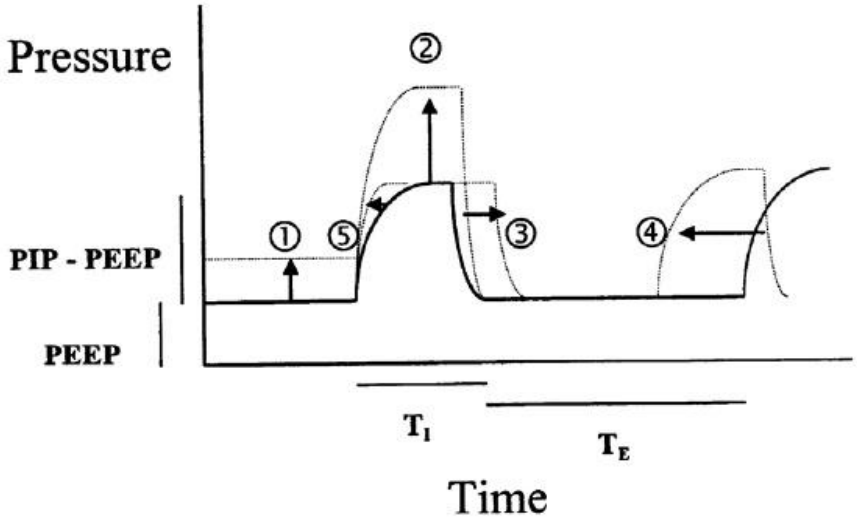
In RDS : require a longer Inspiratory time because the lung will empty rapidly but require more time to fill.

In CLD : decrease vent rate, which allows lengthening the I time and E time.

Inspiratory & Expiratory Time



Mean Airway Pressure

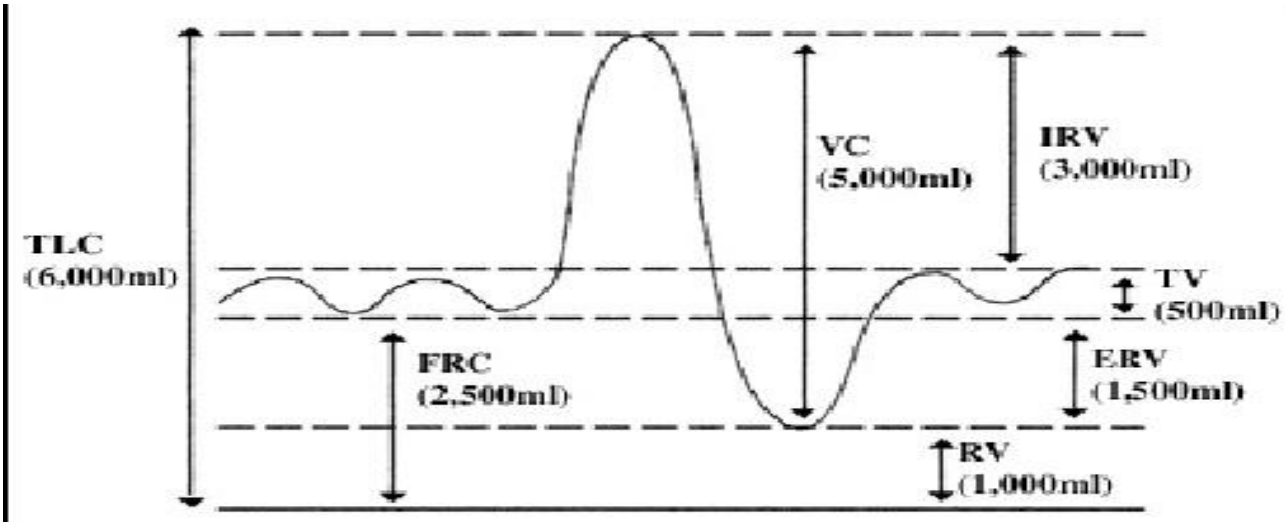


INTERVENTIONS

1. Increase PEEP
2. Increase PIP
3. Increase I/E or T_I
4. Increase Rate
5. Increase Flow

Lung mechanics

- Total lung capacity.
- Tidal volume.
- Functional residual capacity.
- Inspiratory & expiratory reserve volumes
- residual volume.

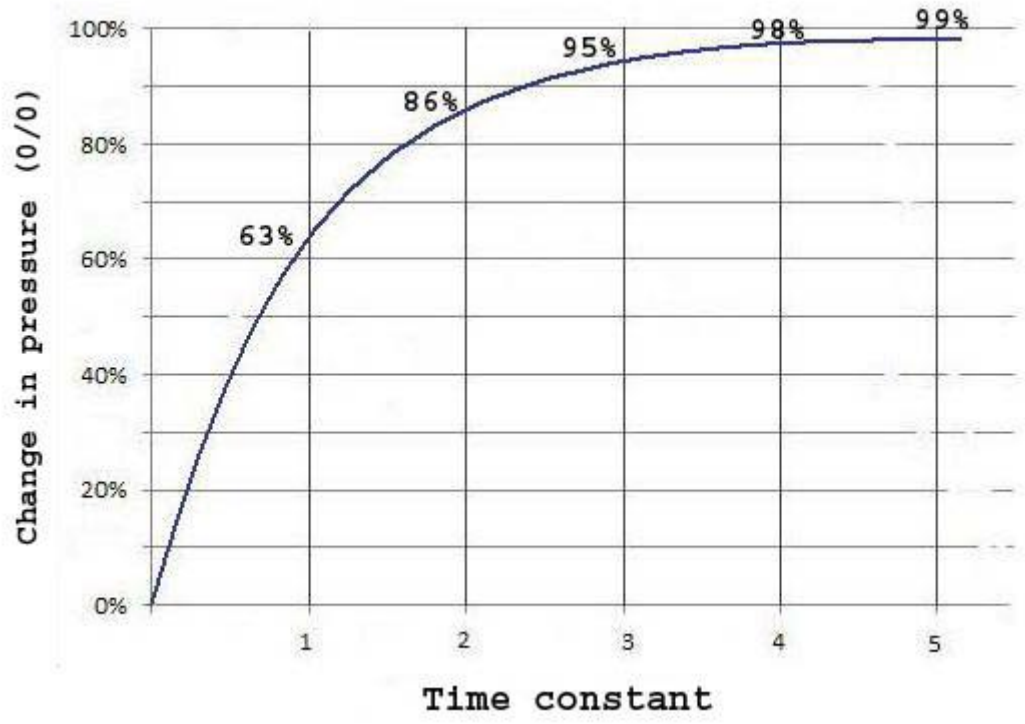


Lung Volumes measured with a spirometer during quiet breathing with one maximum breath. Values shown are for an average-sized healthy young male.

RV	*Residual volume*	*FRC*	*Functional residual capacity*
ERV	*Expiratory reserve volume*	*TV*	*Tidal vlume*
IRV	*Inspiratory reserve volume*	*VC*	*Vital capacity*
TLC	*Total lung capacity*		

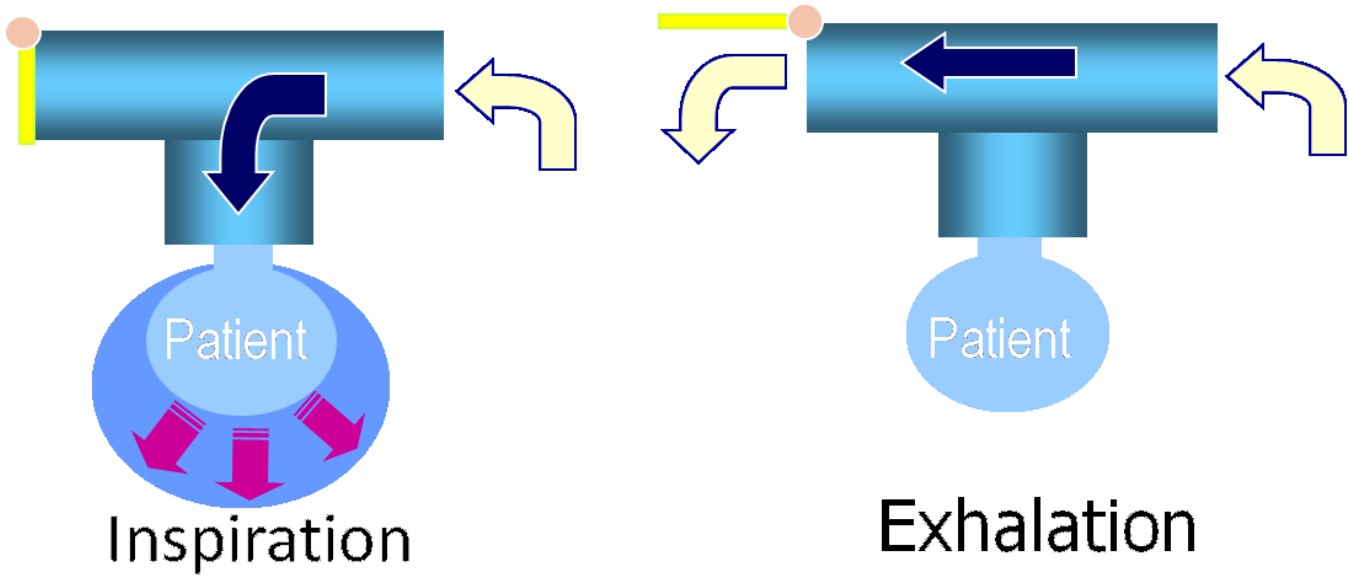
N.B The numbers between ( ) for Adult

Tidal Volume (TV):	The volume of air breathed in and out without conscious effort
Inspiratory Reserve Volume (IRV):	The additional volume of air that can be inhaled with maximum effort after a normal inspiration
Expiratory Reserve Volume (ERV):	The additional volume of air that can be forcibly exhaled after normal exhalation
Vital Capacity (VC):	The total volume of air that can be exhaled after a maximum inhalation: VC = TV + IRV + ERV
Residual Volume (RV):	The volume of air remaining in the lungs after maximum exhalation (the lungs can never be completely emptied)
Total Lung Capacity (TLC):	= VC + RV
Minute Ventilation:	The volume of air breathed in 1 minute: (TV)(breaths/minute)
FRC	*= 30 ml/kg*



Mechanical Ventilation

How does it work



Modes of Ventilation

1. Volume targeted ventilation (VTV)

This is a relatively new form of ventilating newborns.

The delay of use due to technical limitation in measuring the small tidal volumes used.

2. Pressure limited time cycled

Intermittent mandatory ventilation(IMV)

This is a non-synchronised mode of ventilation .

The majority of transport ventilation usethis mode due to technical limitation.

Patient Trigger Ventilation (PTV)

- Ventilator senses infant inspiratory effort and delivers appositive pressure breath.
- Infant inspiratory effort & trigger positive pressure breath can detected by airway flow or pressure or abdominal movement

- Trigger threshold must be reached in order for each positive pressure breath to be delivered
- A back-up ventilation rate is set so that positive pressure breath continue in apneic infant or insufficient inspiratory effort.

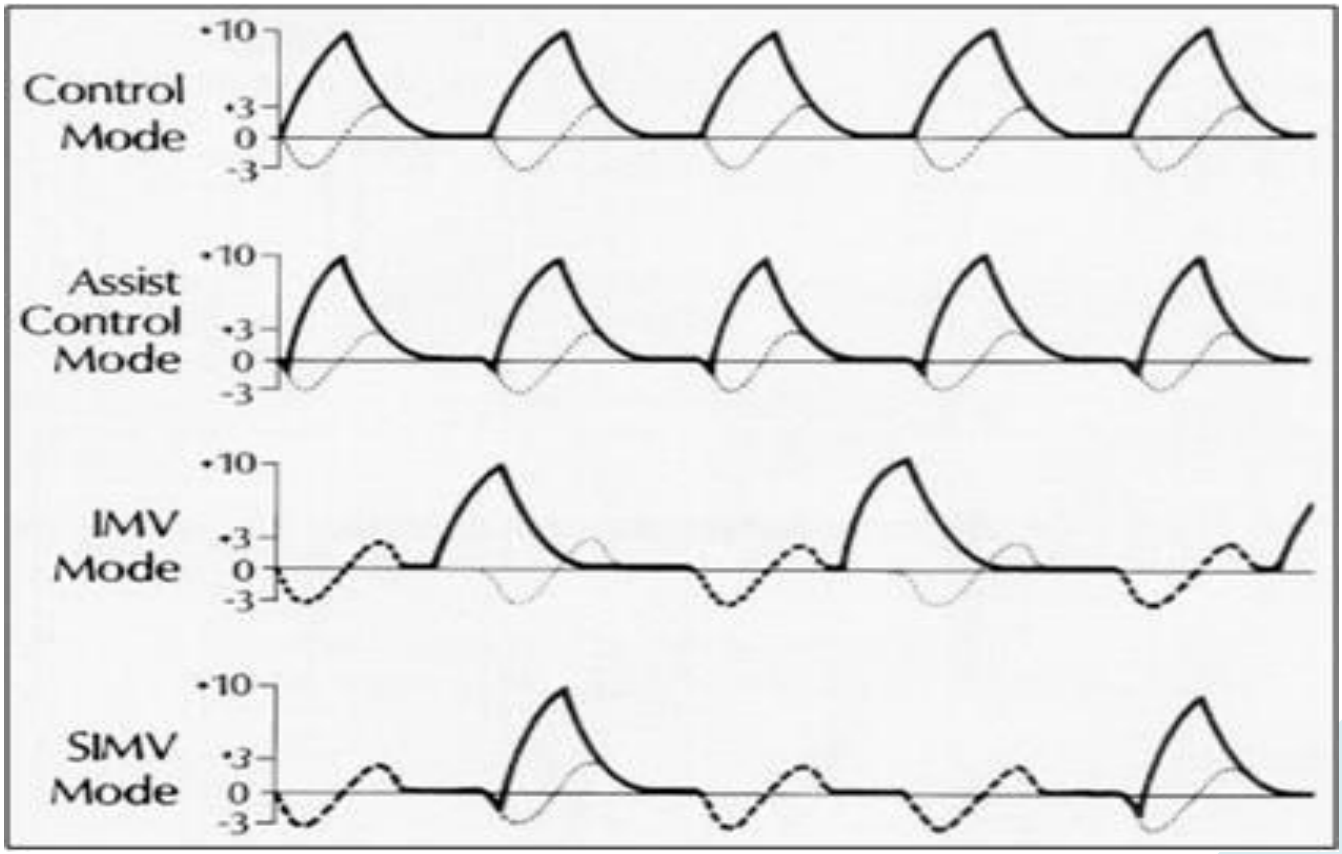
Types of PTV

1. Assist – control (A/C) also called synchronized intermittent positive pressure ventilation(SIPPV).

   A positive pressure breath is delivered each time the infant inspiratory effort exceeds the trigger level.

2. Synchronized intermittent mandatory ventilation(SIMV).

   The number of positive pressure breath are preset any spontaneous breaths above the set rate will not be ventilator assistant .



Advantages of PTV

1. Bettersynchrony help to ↓ patient discomfort .
2. Oxygenation may improve.
3. Possible of air leak ↓ .
4. ↓ Work of breathing.
5. ↓ Duration of ventilation.

If low pco2 on A/C ↓PIP or if already on low PIP consider switching to low rate SIMV (not <20 min) or extubation.

In our unit we use this machine

NEWPORT BREEZE E 150 Ventilator

It is used for ventilatory support of neonates, pediatrics or adults.

The Breeze operates in six basic modes :

Volume control

- A/C + SIGH
- A/C
- SIMV
- Spontaneous

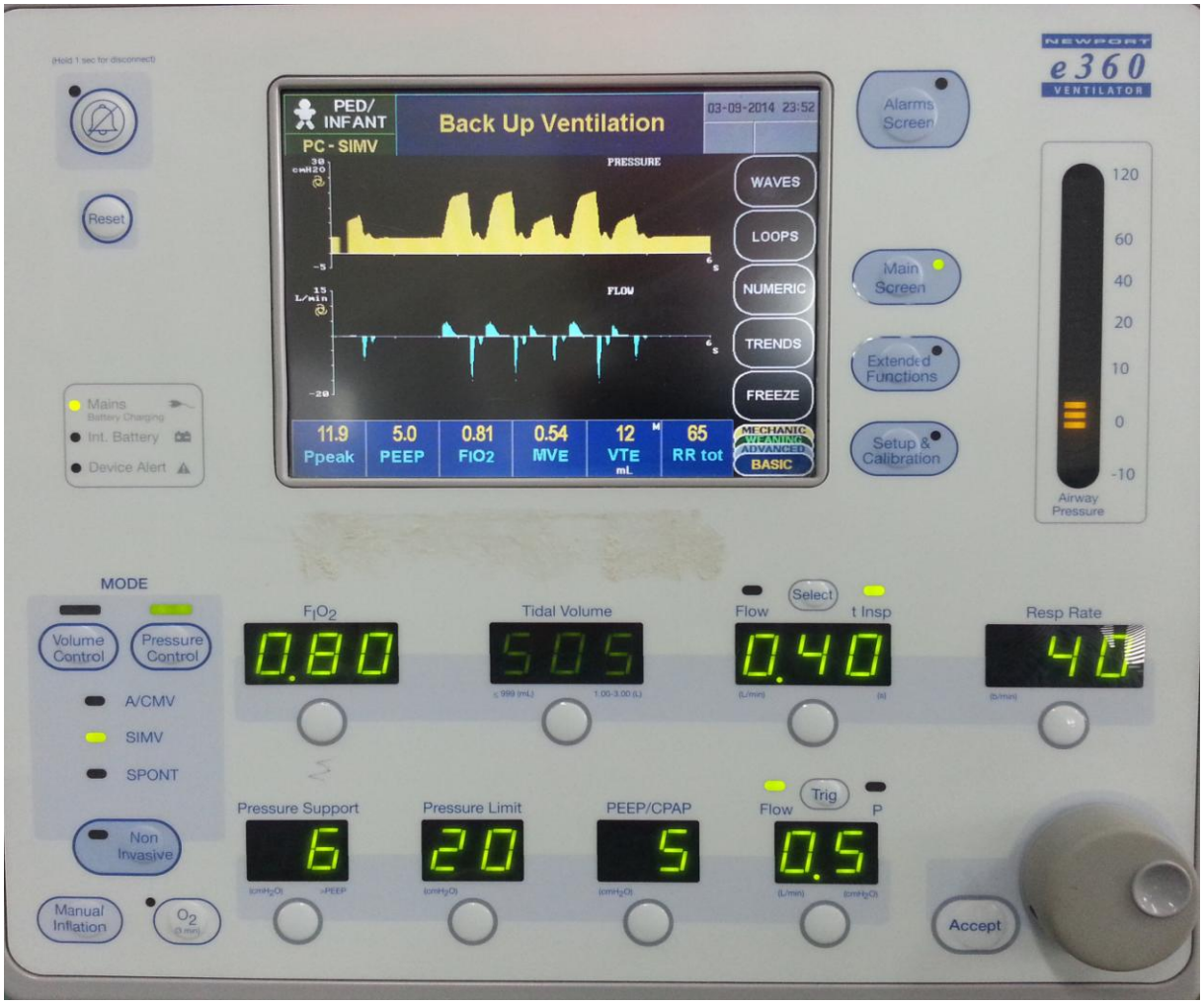
Pressure Control

- Spontaneous.
- SIMV
- A/C

In neonates we use the pressure control mode.

Controls:

FIO2	0.21-1.0 ±3%
Flow	3 -120 L/min
Insp. Time	0.1 – 3.0 sec
Rate	1 – 150 bpm.
Tidal volume	10 – 2000 ml.
PIP	0 – 60 cm H2O
PEEP/CPAP	0 – 60 cm H2O.
Spont. Flow	0 – 50 L/mint.
Trigger Level	-10 – +60 cmH2O



Setting the trigger level

Trigger level is the amount of effort (negative pressure)
to trigger a breath.

Trigger Level knob

A. **Course (pulled out)**

trigger level will be set between -10 to +60 cm H2O.

B. **Fine (Pushed in)**

trigger level will be set between -10 to -5 cm H2O.

The trigger level -1 to -2 cm H2O from the base line (PEEP)

Problem

If the ventilator does not respond to infant inspiratory effort

Possible causes:

- Infant effort too weak.
- Incorrect trigger level
- Leak in circuit.

So we cap off reservoir bag outlet in the first cause, with ↓ Flow and readjust trigger level in the second cause and correct leak in circuit in the third cause.

High Frequency Ventilation (HFV)

Definition:

Ventilation at a high rate at least 2 –4 times the natural breathing rate, using a small TV that is less than anatomic dead space:

Types:

- High Frequency Jet Ventilator (HFJV)
  - Up to 600 breath / min.
- High Frequency Flow Interrupter (HFFI)
  - Up to 1200 breath / min.
- High Frequency Oscillatory Ventilator (HFOV)
  - Up to 3000 / min

Introduction

- The respiratory insufficiency remains one of the major causes of neonatal mortality.
- Intensification of conventional ventilation with higher rates and airway pressures leads to an increased incidence of barotrauma.
- Either ECMO or high-frequency oscillatory ventilation mightresolve such desperate situations.

- Since HFOV was first described by Lunkenheimer in the early
- seventies this method of ventilation has been further developedand is now applied the world over.

Setting

Initial Ventilator Setting

- **Rate** 60/min & adjusted by 5 breath/min also the rate depends on mode of ventilation , avoid R.R of less than 30 in SIMV due to the risk of atelectasis & increase work of breathing.
  This is not a concern of infant on A/C mode.
- **PIP** Intial PIP 18- 20 cmH2o&adgusted by 2 my ↑ to 26 cmH2o according to the disease & if lelow 14 consider extubation.
- **PEEP** 3-8cmH2o usually adjusted by 1cmH2o , High or low level according to the disease.
- **I:E ratio** 1:2 with Ti 0.3-0.5 seconds and related to G.A of neonate.
- **Flow rate** 5-6 L/min.
- **Spontaneaus flow** 4L/ min.
- **Fio2** 60% - 70% & adjusted by 5%.

  N.B. ABG done after 30 min & change sitting acording to ABG.

$$Ti = \frac{\text{G.A in wks}}{100}$$

Settings change as result of ABG

Normal range of arterial blood gas values for term and preterm infants at normal body temperature and assuming normal blood Hb content

	Po2	Pco2	pH	Hco3	BE
Term	80-95	35-45	7.32-7.38	24-26	3.0
Preterm 30-36wks	60-80	35-45-	7.30-7.35	22-25	3.0
Preterm<30 wks	45-60	38-50	7.27-7.32	19-22	4.0

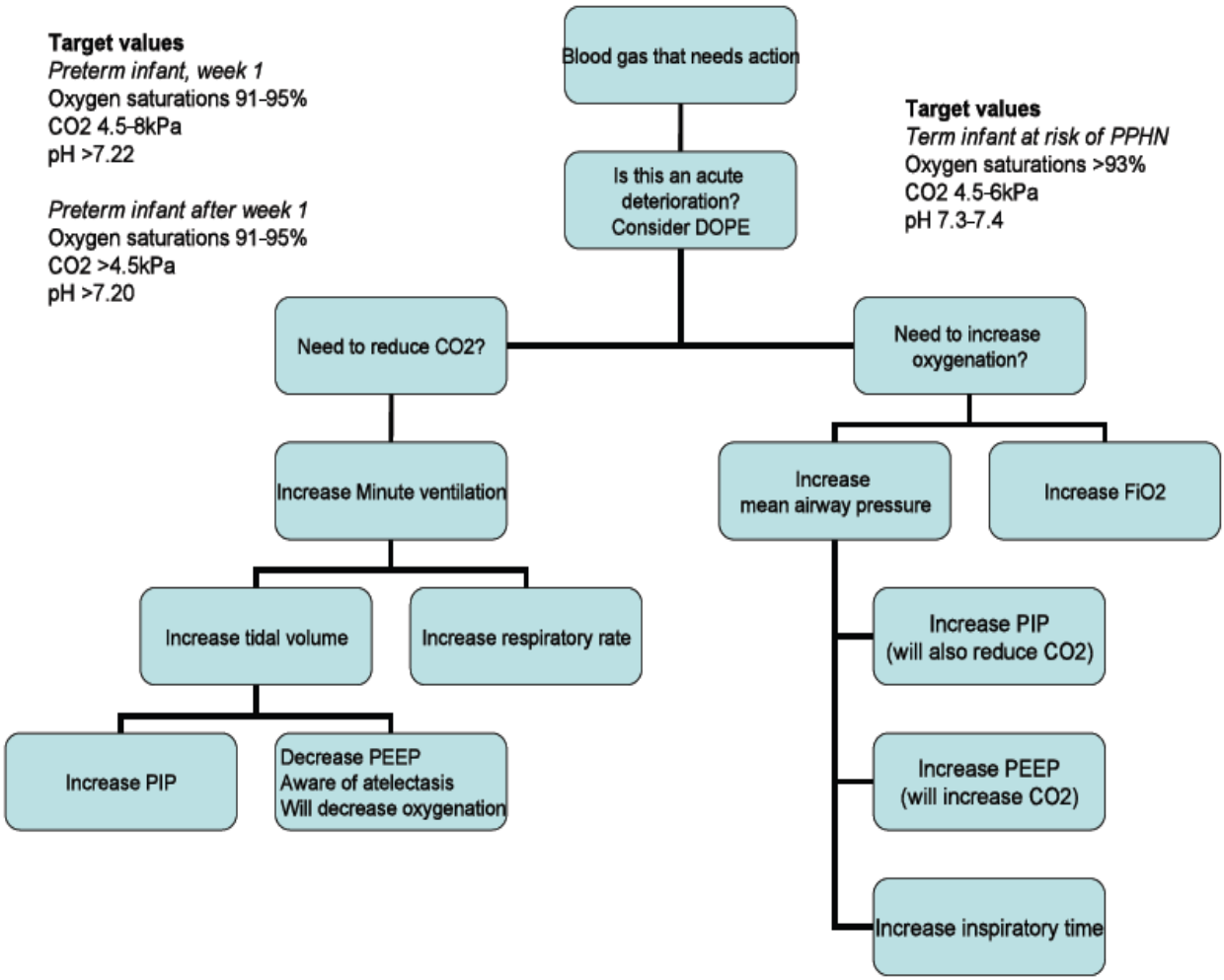
Always do arterial blood gases (venous or capillary blood gases are no value for Po2 and give lower pH & higher pco2 than arterial sample).

Minimum PIP guidelines

Wt in gram	**Minimum PIP**
<750 gram	13
750-1000	14
1001-1500	15
>1500	16

Oxygen saturation target

Infant	Po2(mmHge)	Saturation Range
Preterm<32wks	50-70	88-92%
Preterm≥32wks	60-80	90-95%
Term&Post Term	60-80	90-95%
CLD&PCA>32wks	60-80	90-95%



Ventilator manipulation to increase oxygenation (PaO2)

A. Increasing FIO2:-

- Advantage: less barotrauma ,easy to administer.
- Disadvantage: No effect on V/Q ,oxygen toxicity (PaO2 > 0.60).

B. Increasing PIP :-

- Advantage: Critical opening pressure, improve V/Q.
- Disadvantage: barotrauma, air leak, BPD.

C. Increasing PEEP :-

- Advantage : maintain FRC ,prevent collapse, splint obstructed airways.
- Disadvantages: stiff compliance curve, obstruct venous return, increase expiratory work and CO2, increase dead space.

D. Increasing Ti :

- Advantages: increased MAP without increasing PI
- Disadvantages: Slow rates needed, higher PI, lower minute ventilation.

E. Increasing flow:

- Advantages: Square wave, maximize MAP.
- Disadvantages: More barotrauma, greater resistance at greater flow.

F. Increasing rate :

- Advantages: Increase MAP with lower PI
- Disadvantages: inadvertent PEEP with higher rate or long time constants.

N.B: All the above changes (except FIO2) increase MAP.

Ventilator manipulations to increase ventilation and decrease PaCO2:

A. Increasing rate:-

- Advantage: easy, minimize barotrauma.
- Disadvantage: The same dead space/ tidal volume, inadvertent PEEP.

B. Increasing PIP :-

- Advantage: Improved deed space/tidal volume.
- Disadvantage: more barotrauma, stiff compliance curve.

C. Decreasing PEEP :-

- Advantage: Widen compression pressure, decrease deed space, and decrease expiratory load, steeper compliance curve.
- Disadvantages: decrease MAP, decrease oxygenation, alveolar collapse, stops splinting obstructed / closed airways.

D. ↑ Flow

E. ↑ TE

ABG Score

	0	1	2	3
Ph	>7.3	7.2-7.29	7.1-7.19	<7.1
Po2	>60	50-60	<50	<50
Pco2	<50	50-60	61-70	>71

Score of >3 suggestive ventilator support

Specific disease strategy

1. Respiratory Distress Syndrome (RDS).

a. **Pathophysiology :** decrease compliance & low FRC.

b. **Ventilatory Strategy :**

- Rate ≥ 60 breath/min.
- PIP 13-15. Related to wieght of infant.
- PEEP 4-5 Need to prevent alveolar collapse at end of expiration.

- Ti 0.25-0.4 = 3-5 time constant , related to G.A.
- Permissive hypercarbia Pco2 45-60.

2. Meconium Aspiration (MAS).

a. Pathophysiology : Marked airway resistance, the obstructive phase is followed by inflammatory phase 12-24 hrs.

b. Ventilatory strategy :

- Rate 40-50
- Short Ti
- Long Te to avoid air traping.
- PIP 18/26 may need high pressure if more 30consider HVF.
- PEEP 4-7.
- Ti = 0.45.
- TE need relative long time to avoid air traping.
- FIo2 may need 100%.
- Use sedation

3. Bronchopulmonary Dysplasia (BPD)

a. Pathophysiology :

- ↓ Compliance due to Fibrosis
- ↑ In airway resistance
- Hyperinflation
- ↑ work of breathing .
- V/Q mismatching.

b. Ventilatory strategy :

- Low rate <50.
- PIP low.
- PEEP 6-8.
- Very gradual weaning**.**
- TE relatively prolonged TE need.

4. Apnea

a. Pathophysiology :

- Apnea of prematurity , or during general Anesthesia or neuromuscular paralysis.

b. Ventilatory strategy :

- Normal breathing rate .
- Rate 30-40.
- PIP 12-18.
- PEEP 3-4 cmH2O.
- Fio2 30-40.

5. PPHN

a. Pathophysiology :

- Normal cardio-pulmonary transition fails to occure.
- Marked elevation of pulmonary vascular resistance.

b. Ventilatory strategy :

- Adjust FIo2 to maintain PO2 80-100
- Adjust Rate and PIP to maintain PH (7.35 – 7.45) normal limit.
- Relatively low PEEP 3-4.
- Very gradual weaning in rate &Fio2.
- Sedation.

Oxygenation

Oxygenation of the infant is influenced by the MAP & Fio2.

Oxygenation can be improved by:

1. ↑ FIO2
2. ↑ PIP to ↑ MAP
3. ↑ PEEP to ↑ MAP
4. ↑ Ti

   The target O2saturation88-92%

Carbon Dioxide

The Co2 clearance is affected by alternation in the alveolar minute volume This is the product of Tidal Volume & the rate

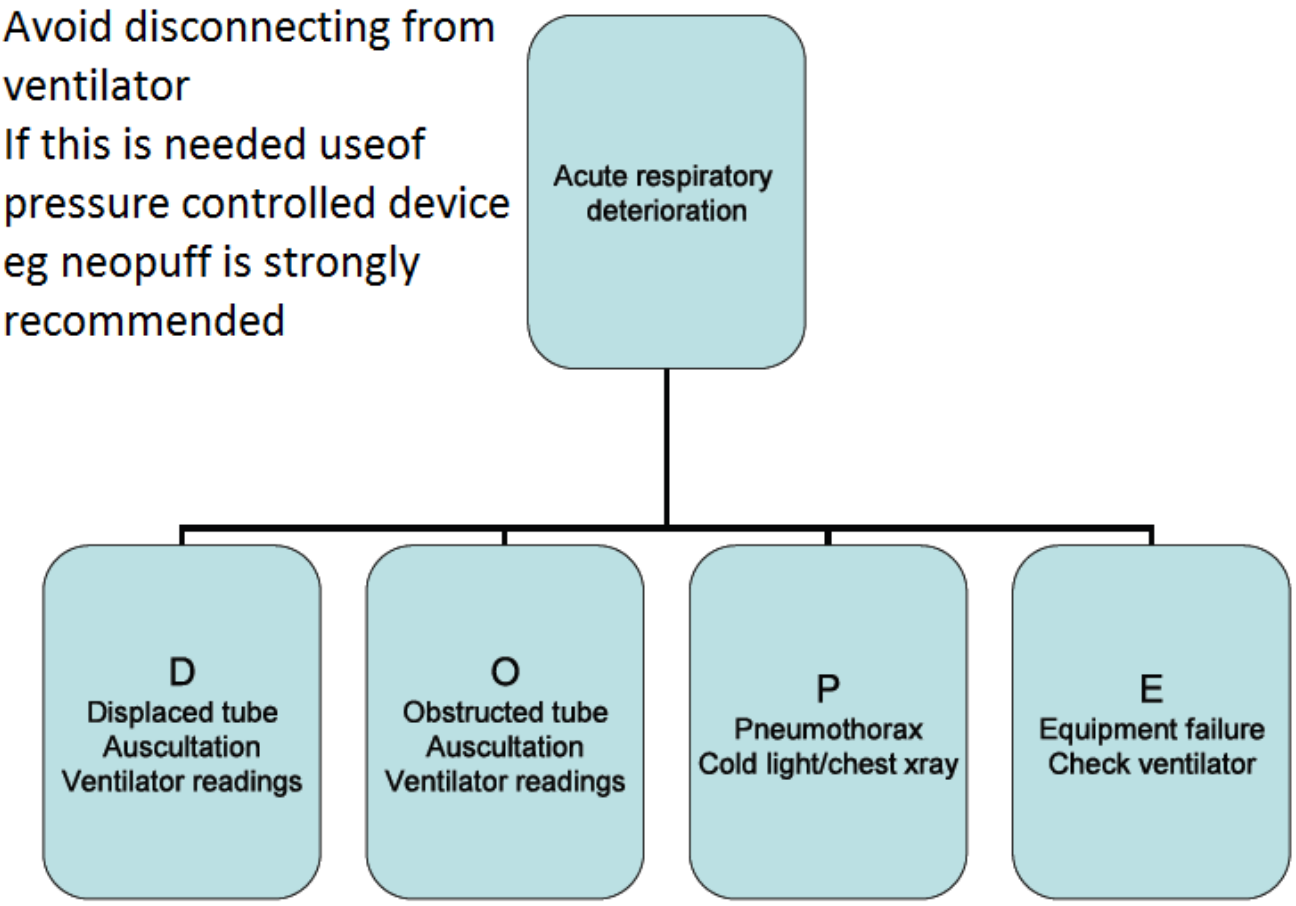
(VTX Respiratory Rate).

Co2 Clearance ↑ by

1. ↑ the VT
2. ↑ PIP
3. ↑ the Rate to avoid atelectasis

Co2 can ↑ by

1. ↓ VT
2. ↓ PIP
3. ↓ Rate
4. ↑ PEEP
5. Co2 target (34-60 mmHg)



Weaning from Mechanical Ventilation & Extubation

Criteria for weaning

- Adequate oxygenation Po2≥ 60 at FIo2 ≤ 40
- Po2/ FIo2≥ 150-300.
- Stable C.V.S Heart Rate & Blood Pressure.
- Afebrile.
- No significant respiratory acidosis.
- Adequate Hb (≥ 8-10).
- No sedation & Alert.

- Stable metabolic status .
- Resolution of disease acute phase .
- Fio2 is weaned related to ABG ≤Fio230 .
- PIP weaned first gradually to (15-10 cmH2o).
- PEEP 3-4 cmH2o.
- Respiratory Rate ↓ gradually < 10-15.
- The smaller the baby the slower the weaning process.
- Stop sedation & Analgesia from respiratory rate below 20 .
- VLBW better to extubate from rate 10 / breath /min.

To Nasal CPAP as ETT CPAP Exhausts the preterm infant.

N.B In A/C mode weaning by ↓ FIo2 and PIP.

In SIMV by ↓ FIo2 and Rate.

Risk factor for Extubation failure

- Low GA (< 28 wks.).
- Prolonged ventilation (10-14 days).
- History of previous Extubationfailure .
- Used of sedation.
- Multiple reintubation .
- Evidence of residual lung injury (PBD), Emphysema.
- Extubation from High setting Rate,HighFIo2.
- PDA.

Criteria For Reintubation

- Severe apnea requiring positive pressure ventilation .
- Multiple episodes of of apnea > 6 within 6 hrs.
- Hypoxemia FIO2 >50% to maintain O2 saturation >88%.
- Hypercapnia >60 with pH<7.25 .
- Severe chest retraction and increase work of breathing.

To Facilitate Extubation

- **Caffein:**IV before Extubation6-12hrs. (Not available so use Aminophyllin)
- **Dexamethasone:**Smalldoses (0.2mg/kg/day) Begin 6-8 hrsbeforeextubation for 2 days.
- **Nebulized racemic Epinephrine &Decort** may be useful for stridor after Extubation but no enough data Available for its use.
- NPO 6-12 hrs.(no feeding).
- CXR follow up.
- N.B Nasal CPAP used after Extubation of infants <30 wks to avoid reintubation.

Complication of MV

Air way injury

- Tracheal inflammation
- Subglottic stenosis
- Granuloma formation
- Palatal grooving
- Nasal septal injury .

Air Leaks

- Pneumothorax
- Pulmonary Interstitial emphysema.
- Pnemomediastinum.

Cardiovascular

- ↓ Cardiac output.
- PDA.

Chronic lung injury

- BPD.
- Acquired lobar emphysema.

Others

- ROP.
- Apnea.
- Infection.
- Feeding intolerance.
- IVH.
- Developmental delay.
- Hyperinflation.

Surfactant

Surfactant Replacement Therapy

- Together with antenatal corticosteroid administration, surfactant replacement therapy is the most important therapeutic advance in neonatal care in the last decade
- Early administration of selective surfactant decreases risk of acute pulmonary injury and neonatal mortality
- Multiple doses result in greater improvements in oxygenation and ventilator requirements, a decreased risk of pneumothorax, and a trend toward improved survival.

Indication

Prophylaxis (administration within 15 min of birth)

Babies born ≤26 weeks gestation

- Electively intubate and give surfactant as prophylaxis Babies born at 27–28+6 weeks' gestation
- If require intubation for respiratory support during resuscitation/stabilisation, give surfactant as prophylaxis

Early rescue treatment

Babies born at 27–28+6 weeks' gestation

- If require intubation for respiratory distress, give surfactant early (within 2 hr of birth)

All other babies requiring intubation and needing FiO2 >0.3 for surfactant deficiency

disease i.e. continuing respiratory distress AND evidence of RDS on chest X-ray

- Give rescue surfactant

Other babies that can be considered for surfactant therapy (after senior discussion)

- Ventilated babies with meconium aspiration syndrome
- Term babies with pneumonia and stiff lungs

Contraindication

Discuss use in babies with massive pulmonary haemorrhage with neonatal consultant.

Equipment

- Natural surfactant, Poractantalfa (Infasurf) 6 ml each ml contain 35 mg dose 3ml /kg.

- whole vial; prophylaxis and rescue doses of Curosurf can differ, check dose with local policy.
- Sterile gloves.
- Trach Care Mac catheter [do not cut nasogastric (NG) tube]

Procedure

Preparation

- Calculate dose of surfactant required and warm to room temperature.
- Ensure correct endotracheal tube (ETT) position.
- Check ETT length at lips.
- Listen for bilateral air entry and look for chest movement.
- If in doubt, ensure ETT in trachea using laryngoscope and adjust to ensure bilateral equal air entry.
- Chest X-ray not necessary before first dose
- Refer to manufacturer's guidelines and Neonatal Formulary
- Invert surfactant vial gently several times, without shaking, to re-suspend the material.
- Draw up required dose Surfactant 2011-13.
- Administer via Trach Care Mac device (note: it is no longer acceptable to administer surfactant via a nasogastric feeding tube as this contravenes European conformity (CEmarking) and NPSA 19)

Instillation

- With baby supine, instil prescribed dose down tracheal tube; give 2 boluses of Poractantalfa.

- Wait for recovery of air entry/chest movement and oxygenation between boluses.

Post-instillation care

- Do not suction ETT for 8 hr [suction is contraindicated in Surfactant Deficiency Disease (SDD) for 48 hr].
- Be ready to adjust ventilator/oxygen settings in response to changes in chest movement, tidal volume and oxygen saturation.
- Take an arterial/capillary blood gas within 30 min.

Subsecuent Managment

- If baby remains ventilated at FiO2 >0.3 with a mean airway pressure of >7 cm of water, give further dose of surfactant.
- Poractantalfa after 6–12 hr.
- 3rd dose can be given only at the request of the attending neonatal consultant.

Documentation

- For every dose given, document in case notes:
- indication for surfactant use.
- time of administration.
- dose given.
- condition of baby pre-administration, including measurement of blood gas unless on labourward when saturations should be noted.
- response to surfactant, including measurement of post-administration blood gas and saturations.
- reasons why second dose not given, if applicable.
- reason(s) for giving 3rd dose if administered.

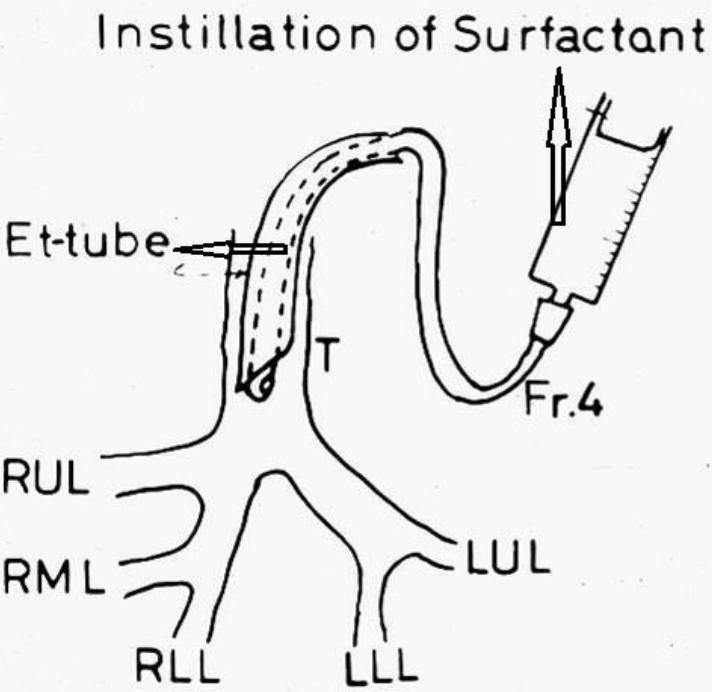


Figure 6. Diagrammatic presentation of instillation of endotracheal instillation of surfactant solution into lungs. The figure shows the syringe containing the surfactant suspension attached to F 4 feeding tube inserted into the trachea (*T*) via the endotracheal tube (*ET tube*). *Key*: *RUL*, right upper lobe; *RML*, right middle lobe; *RLL*, right lower lung; *LUL*, left upper lung; *LLL*, left lower lung.

Related drugs

FENTANYL (Sublimaze)

Dose and Administration

a. Sedation and analgesia: 1-4 micrograms/kg/dose IV slow push, IM.
    1. For intubation, use 4micrograms/kg
    2. Repeat as required (usually every 2-4 hours).
    3. May be given as a continuous infusion: 1-5 micrograms/kg/hour.
b. Anaesthesia: 5-50 micrograms/kg/dose.
    1. Minor surgery 5-20 micrograms/kg/dose.
    2. Major surgery 30-50 micrograms/kg/dose.

$$\text{Fentanyl (micrograms) in 50ml IV solution} = \frac{50 \times \text{weight (kg)} \times \text{dose (micrograms/kg/hour)}}{\text{IV rate (ml/hour)}}$$

Usual strength = 2-10 micrograms/ml.

Indications

1. Intubation
2. Analgesia
3. Sedation
4. Anaesthesia

Contraindications and Precautions

1. Known hypersensitivity to fentanyl and/or other opiates.
2. Bradyarrhythmias.
3. Myasthenia gravis
4. Caution in preterm infants, especially extreme immaturity.
5. Caution in neonates with hepatic or renal impairment

6. Caution in nonventilated neonates with respiratory distress.
7. Caution in neonates with raised intracranial pressure.

Clinical Pharmacology

Fentanyl citrate, a narcotic analgesic, is 50-100 times more potent than morphine. Actions qualitatively similar to those of morphine. Produces a minimum of cortical depression. Alterations in respiratory rate and alveolar ventilation may last longer than analgesic effect. No significant cardiovascular effects at usual therapeutic doses.

Rapid distribution with sequestration in fat. Wide variability in distribution volume (Vd 1-13 L/kg). Extensive binding to human plasma protein. Hepatic metabolism. Excretion via the kidney. Elimination half-life very variable in neonates (6-32 hours). Onset of action almost immediate with IV administration (7-8 minutes with IM). Peak effect 5-15 minutes following IV injection. Duration of the analgesic effect 30-60 minutes (1-2 hours with IM).

Possible Adverse Effects

1. Bradycardia (rapid administration).
2. Respiratory depression.
3. Decrease in physical activity.
4. Physical dependence.
5. Rapid tolerance with prolonged use (>2 days).
6. Nausea and vomiting.
7. Severe muscle rigidity, especially chest wall rigidity. Can be avoided with slow IV pushes rather than rapid boluses. Have suxamethonium ready.

Special Considerations

1. Faster onset of action but shorter duration of action than morphine.
2. Additive effects with other narcotics and/or other central nervous system depressants.
3. With prolonged use the minimum effective dose may increase as tolerance develops.
4. After continuous use, discontinue fentanyl over a few days because physical dependence develops.
5. Management of fentanyl overdose and/or toxicity: discontinue fentanyl, supportive therapy (ventilation, etc.), naloxone (0.01-0.1 mg/kg/dose IV).

MIDAZOLAM (Hypnovel)

Dose and Administration

1. **Slow IV push**
   50 to 150 micrograms/kg as a slow push over 5 minutes. Can be repeated Q2-4H as required.
   Give lower dose if opiates being administered simultaneously.
2. **Continuous intravenous infusion**
   10-60 micrograms/kg/hour. Dosage can be increased if necessary.

$$\text{Midazolam (micrograms) in 50ml IV solution} = \frac{50 \times \text{weight (kg)} \times \text{dose (micrograms/kg/hour)}}{\text{IV rate ml/hour}}$$

Indications

1. Sedation/anaesthesia.
2. Anticonvulsant (3^{rd} or 4^{th} line).

Contraindications and Precautions

1. Known hypersensitivity to midazolam.
2. Shock.
3. Caution in preterm infants, especially extreme immaturity.
4. Caution in neonates with hepatic or renal impairment.
5. Caution when concurrent use with opiates, particularly fentanyl.
6. Caution when concurrent use with other anticonvulsants.

Interactions

1. Concurrent administration with erythromycin promotes accumulation.
2. May alter the depth of and prolong the recovery from concurrent neuromuscular blockade.
3. Xanthines may decrease the anaesthetic/sedative effect of benzodiazepines. Care needs to be taken with adding or withdrawing caffeine or aminophylline.

Clinical Pharmacology

Midazolam, an imidazobenzodiazepine, has anxiolytic, sedative, muscle relaxant and anticonvulsant actions. Facilitates the action in the brain of gamma aminobutyric acid, a naturally occurring neurotransmitter. Absorption 30% with oral and 50% with nasal administration. Rapid and extensive distribution. Highly protein bound. Hepatic metabolism to active and inactive derivatives, impaired by poor hepatic perfusion . Very slow elimination via the kidneys. Elimination half-life variable (6-7 hours in infants close to term, longer in less mature infants), with the major metabolite (1-hydroxymidazolam) having an even shorter half-life. Rapid onset of action (<3 minutes) and peak sedative action <20 minutes after IV administration. Anticonvulsant action may be more rapid. The IV preparation has a pH of 3.

Possible Adverse Effects

1. Hypotension and reduced cardiac output, particularly when used in combination with fentanyl.
2. Respiratory depression and apnoea.
3. Hypotonia.
4. Seizures or seizure-like activity may be seen following rapid bolus administration and in patients with underlying CNS disorders.

5. Cerebral blood flow velocities are reported to decrease transiently in preterm infants receiving midazolam boluses, possibly reflecting the reduction in blood pressure.
6. Nasal administration in children and adults has been reported to produce a burning sensation.

Special Considerations

1. Lower doses of midazolam should be considered in neonates with reduced cardiac output.
2. Development of tolerance and a requirement for higher doses may occur with prolonged use.
3. Prolonged use may result in neonatal abstinence syndrome.
4. Recent systematic review has suggested that routine use of midazolam for sedation in ventilated infants is associated with an increased incidence of adverse neurological outcomes. [9]
5. Management of midazolam overdose and/or toxicity: stop midazolam, supportive therapy (ventilation, volume expansion etc.), consider use of specific antagonist flumazenil (very limited experience in the neonate).

PROSTAGLANDIN E1 (ALPROSTADIL)

Paediatric Prostin VR

Dose and Administration

1. 5 to 100 nanograms/kg/minute (0.005-0.1 micrograms/kg/minute) by continuous intravenous infusion.
2. Start with low infusion rate and titrate according to the infant's response. Higher initial doses are usually no more effective and have a higher incidence of adverse effects.
3. Maintenance dose may be as low as 5 nanograms/kg/minute (0.005 micrograms/kg/minute).

$$\text{Prostaglandin (micrograms) in 50ml IV} \quad \frac{3 \times \text{weight (kg)} \times \text{dose (nanograms/kg/min)}}{}$$

solution = IV rate (ml/hr)

Usual dilution 3 - 6 micrograms/ml. In rare situations the strength can be made up to 20 micrograms/ml. This is however very hyperosmolar. At 3 micrograms/ml, 1ml/hour = 0.05 micrograms/minute.

Indications

Dilatation of ductus arteriosus in infants with ductal dependent congenital heart defects:

1. Transposition of the great vessels.
2. All right sided cyanotic congenital heart defects associated with reduced pulmonary perfusion.
3. Left sided congenital heart defects including hypoplastic left heart syndrome, coarctation of aorta and interrupted aortic arch.

Contraindications

1. None.

Precautions

1. Respiratory distress. Alprostadil (Prostaglandin E1) should not be used in neonates with Respiratory Distress.3
2. Total anomalous venous return with obstruction.
3. Infants with bleeding tendencies (Alprostadil inhibits platelet aggregation).
4. Seizure disorders.

Clinical Pharmacology

Prostaglandin E1 is a potent vasodilator of all arterioles. Other effects include inhibition of platelet aggregation, and stimulation of uterine and intestinal small muscle. Alprostadil (Prostaglandin E1) is rapidly cleared by metabolism, primarily occurring in the lungs, and excretion via the kidney. 3 Maximal drug effect usually seen within 30 minutes in cyanotic lesion: may take several hours in acyanotic lesions.

Possible Adverse Effects

1. Apnoea.
2. Hypotension.
3. Hyperthermia (transient).
4. Hypoglycaemia.
5. Tachycardia.
6. Bradycardia.
7. Seizures.
8. Diarrhoea.
9. Skin flush secondary to vasodilation- occurs more frequently with intraarterial administration.
10. Sepsis, cardiac arrest, disseminated intravascular coagulation, hypokalaemia, oedema, cortical proliferation of the long bones.

Special Considerations

- Alprostadil (Prostaglandin E1) is rapidly metabolised and must, therefore, always be given by continuous intravenous infusion. Vascular access must be secure at all times and may demand the insertion of a central venous catheter or long line to ensure continuity of delivery.

- The maintenance dose of the Alprostadil (Prostaglandin E1) infusion is determined by titration according to the infant's response - oxygenation versus adverse effects.
- Monitor:
    - Observe respiratory effort closely
    - Monitor arterial pressure closely. If arterial pressure falls, a bolus of fluid (10- 20 ml/kg) is required. It may be necessary to decrease the rate of infusion.
    - Pulse oximetry is mandatory due to risk of apnoea and to monitor therapeutic effect in cyanotic heart disease.
    - Where there is restricted systemic blood flow, measure efficacy by monitoring improvement of systemic blood pressure and blood pH, and femoral pulses/arm-leg BP gradient in aortic coarctation.
    - Renal function; full Blood Count & platelets frequently.
- Increased infant temperature is not an indication to stop therapy.

DOAMINE HYDROCHLORIDE

Dopamine DBL, Dopamin

Dose and Administration

1. 2-20 micrograms/kg/minute by continuous IV infusion1.
2. Begin at a low dose and titrate by monitoring clinical response.
3. Maximum recommended dose 20 micrograms/kg/minute2.
4. If doses greater than 10 – 15 micrograms/kg/min are required then dobutamine or noradrenaline may be added1.
5. Administer via a central line (UVC, Longline, or Surgical CVL). If no central access available, use a large vein.

6. Usual dilution 30 mg/kg (0.75 ml/kg) dopamine to make 50 ml with Normal Saline or D5W
   1 ml/hour = 10 micrograms/kg/minute.

$$\text{Dopamine (mg) in 50ml IV solution} = \frac{3 \times \text{weight (kg)} \times \text{dose (micrograms/kg/min)}}{\text{IV Rate (ml/hr)}}$$

Indications

1. To improve cardiac output, blood pressure and urine output in critically ill infants with hypotension.

Contraindications

1. Hypersensitivity to sympathomimetic amines and sulfites.
2. Uncorrected tachyarrhythmias.

Precautions

1. Hypovolaemia- correct before commencing dopamine
2. Hyperthyroidism
3. Caution if administration concurrent with phenytoin.

Clinical Pharmacology

Dopamine is a sympathomimetic catecholamine which exhibits alpha adrenergic, beta adrenergic, and dopaminergic agonism. The mechanism of action in neonates is controversial. Relative effects of dopamine at different doses are uncertain because of developmental differences in:

1. endogenous noradrenaline stores
2. alpha and beta adrenergic, and dopaminergic receptor functions
3. the ability of the neonatal heart to increase stroke volume.
   Responses tend to be individualised.

Dopamine is metabolised very rapidly and is effective only when administered intravenously by continuous infusion. The half-life of dopamine effect is 2 minutes, which is the same as the other catecholamines. No information available on protein binding. 97% is excreted in the urine as metabolites.

Drug effects are dose dependent:

1. Low dose: 2-5 micrograms/kg/minute. Little effect seen on heart rate or cardiac output. Increased blood flow accompanied by increased urine output.
2. Intermediate doses: 5-15 micrograms/kg/minute. An increase in cardiac contractility and cardiac output results in increased normal blood flow and heart rate.
3. High dose: 15 micrograms/kg/minute. Alpha adrenergic effects begin to dominate: increased systemic and pulmonary vascular resistance,a decrease in blood flow, and a reduction in cardiac output in the neonate especially in the first few days of life3. Decrease in normal perfusion.

Possible Adverse Effects

1. Venous irritation, soft tissue injury at the site of IV injection.
2. Vomiting, tachycardia, vasoconstriction, hypotension.
3. Infusions > 20 micrograms/kg/minute are associated with an increased risk of dysrhythmias eg. tachycardia and, bradycardia, and vasoconstriction1
4. Less common: bradycardia, hypertension.

Special Considerations

1. Dosage range is determined by type of desired clinical effect. Start at the lower end of the desired range and titrate according to clinical response.
2. Volume loading is considered before commencing dopamine infusion.
3. Use with caution in patients with persistent pulmonary hypertension of the newborn.
4. Suggested treatment for tissue sloughing following IV infiltration: inject a1mg/ml solution of phentolamine into the affected area. The usual amount needed is 1-5 ml, depending on the size of the infiltrate.
5. Dopamine effects are prolonged and intensified by beta blockers.
6. General anaesthetic: increased risk of arrhythmias or hypertension.
7. Phenytoin may lower blood pressure.
8. Acidosis decreases effectiveness of dopamine.
9. Administration via the UAC is not recommended.

MAGNESIUM SULPHATE (Magnesium)

Dose and Administration

Initial Dose

1. 200mg/kg dose.
2. Dilute to 8% concentrate in D5W. Infuse IV for 30 minutes. DO NOT exceed 150 mg/minute.

Continuous IV infusion

1. 20 - 50mg/kg/hour. Dilute to 8% concentration in D5W.
2. Usual dilution 4 grams magnesium sulphate to make 50ml with D5W = 80mg/ml
   0.25ml x weight = 20mg/kg/hour

Indications

1. Seizures refactory to other anticonvulsant therapy.
2. Hypomagnesaemia.
3. Severe persistent pulmonary hypertension of the newborn unresponsive to other vasodilation management.

Contraindications and Precautions

1. Patients with heart block or myocardial damage.
2. CAUTION in patients with impaired renal function and/or electrolyte imbalance.

Clinical Pharmacology

At high serum concentrations Mg is a potent vasodilator, muscle relaxant and sedative. Magnesium is the second most common intracellular cation. One half of body Mg is in bone, one-fourth is in muscle and one-fourth is in soft tissue. About 25% to 30% of total plasma Mg is bound to protein, 10% to 15% circulates in complex form and 55% to 60% is ionised.

Readily crosses the placenta and is distributed in mothers milk, however breastfeeding is not contraindicated. In the newborn Mg absorption occurs in the small intestine: 55% to 75% of ingested Mg normally is absorbed. The main route of Mg loss is through the kidneys. Serum magnesium concentrations are maintained within a narrow range. At the three major target organs for hormonal control of Mg homeostasis (bone, intestine and kidney) the close inter-relationship between Mg and Ca is evident.

An elimination half life of 43.2 hours has been reported in newborn infants whose mothers received magnesium sulphate. The elimination rate is the same for both preterm and term infants.

Possible Adverse Effects

1. ECG changes (prolongation of the atrio-ventricular conduction time, sinoatrial block and atrio-ventricular block).
2. Circulatory collapse, hypotension.
3. Gastrointestinal disturbances (diarrhoea, abdominal distension, absence of bowel sounds).
4. Urinary retention.
5. CNS depression (central sedation, muscle relaxation, hyporeflexia and decreased excitability).
6. Calcium and potassium disturbances.
7. Respiratory depression.

Special Considerations

1. Anticipate change in calcium and phosphorus balance.
2. Drug interaction has been reported between magnesium sulphate and gentamicin (respiratory arrest).
3. Monitor serum magnesium and calcium levels.
4. Antidote for hypermagnesaemia is calcium gluconate.

References

Intubation (neonatal guidelines 2011-2013).

Basic terminology M.V.

Lung physiology & mechanics.

Modes of ventilation (oxfored 2012).

Setting om M.V (north trent neonatal guidelines).

Drugs (NM newborn drug protocol).

Surfactant (neonatal guidelines 2011- 2013).

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